DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

TRANSMITTED BY FACSIMILE **March 26, 2009**

Nadine D. Cohen, Ph.D.
Senior Vice President, Regulatory Affairs
Biogen Idec
14 Cambridge Center
Cambridge, MA 02142

RE: BLA 125104
TYSABRI (natalizumab) injection for intravenous use
MACMIS # 17314

Dear Dr. Cohen:

As part of its monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) of the U.S. Food and Drug Administration (FDA) has reviewed Biogen Idec's (Biogen) sponsored links on internet search engines (e.g., Google.com) for TYSABRI (natalizumab). The sponsored links are misleading because they make representations and/or suggestions about the efficacy of TYSABRI, but fail to communicate **any** risk information associated with the use of this product. In addition, the sponsored links inadequately communicate TYSABRI's indication and fail to use the required established name. Thus, the sponsored links misbrand TYSABRI in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and FDA implementing regulations. *See* 21 U.S.C. 352(a) & (n), 321(n); 21 CFR 201.10(g)(1), 202.1(b)(1), (e)(3)(i), (ii) & (e)(6)(i).

Background

According to its FDA approved product labeling (PI):

> TYSABRI is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis to delay the accumulation of physical disability and reduce the frequency of clinical exacerbations . . . . Because TYSABRI increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability, TYSABRI is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, alternate multiple sclerosis therapies [see *Boxed Warning, Warnings and Precautions . . .*].

TYSABRI is associated with major risks as reflected in the Boxed Warning, Contraindications, Warnings and Precautions, and Adverse Reactions section of the PI. Moreover, because of the risk of PML, a consequence of TYSABRI use that is fatal or severely debilitating, TYSABRI is available only through a special restricted distribution program.

Omission of Risk Information

Promotional materials, other than reminder pieces, which include the name of the drug product but do not include indications or other representations or suggestions relative to the drug product (see 21 CFR 200.200, 201.100(f), 202.1(e)(2)(i)), are required to disclose risk and other information about the drug. Such materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to consequences that may result from the use of the drug as recommended or suggested by the materials. The sponsored links present the following claims about TYSABRI for the treatment of multiple sclerosis (MS) (underlined emphasis in original):

- Multiple Sclerosis?
  Satisfied with your MS Medication or Looking for Something Different?
  www.Tysabri.com

- Multiple Sclerosis – MS
  A Multiple Sclerosis Treatment That's Different from the Others.
  www.Tysabri.com

These sponsored links, however, fail to communicate **any** risk information, and their casual approach to TYSABRI treatment is extraordinary in light of the potentially lethal risks of the drug and the stringent controls over its distribution. For promotional materials to be truthful and non-misleading, they must contain risk information in each part as necessary to qualify any representations and/or suggestions made in that part about the drug. By omitting the most serious and frequently occurring risks associated with the drug, the sponsored links misleadingly suggest that TYSABRI is safer than it is known to be. We note that these sponsored links contain a link to the product's website, www.Tysabri.com. However, this does not mitigate the misleading omission of risk information from these promotional materials.

Inadequate Communication of Indication

The above sponsored links for TYSABRI provide a very brief statement about what the drug is for; however, this statement is incomplete and misleading, suggesting that TYSABRI is useful in a broader range of conditions or patients than has been demonstrated by substantial evidence or substantial clinical experience.

Specifically, the sponsored links for TYSABRI present unqualified claims about the use of TYSABRI for the treatment of MS, such as "A Multiple Sclerosis Treatment That's Different from the Others," misleadingly implying that this drug product is indicated for **all** patients with multiple sclerosis, when this is not the case. As reflected in the Background section (above), the indication for TYSABRI includes specific limitations, and it is not indicated broadly for all patients with multiple sclerosis. The sponsored links fail to disclose any of the limitations to the drug's indication, thereby broadening the indication for the drug.

Failure to Use Required Established Name

The sponsored links fail to present the full established name for TYSABRI, despite the requirement to do so. *See* 21 CFR 201.10(g)(1) & 202.1(b)(1).

Conclusions and Requested Action

For the reasons discussed above, the sponsored links misbrand TYSABRI in violation of the Act and FDA regulations. *See* 21 U.S.C. 352(a) & (n), 321(n); 21 CFR 201.10(g)(1), 202.1(b)(1), (e)(3)(i), (ii) & (e)(6)(i).

DDMAC requests that Biogen immediately cease the dissemination of violative promotional materials for TYSABRI, such as those described above. Please submit a written response to this letter on or before April 9, 2009, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) in use for TYSABRI as of the date of this letter, identifying which of these materials contain violations such as those described above, and explaining your plan for discontinuing use of such materials. Finally, we encourage you to review your promotional materials for the other prescription drug products that Biogen promotes in the United States and to discontinue or revise any materials with the same or similar violations, and request that your response address this issue as well.

Please direct your response to the undersigned at the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, 5901-B Ammendale Road, Beltsville, MD, facsimile at 301-847-8444. In all future correspondence regarding this matter, please refer to MACMIS # 17314 in addition to the BLA number. We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for TYSABRI comply with each applicable requirement of the Act and FDA implementing regulations.

Sincerely,

/S/

Sharon Watson, PharmD
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications